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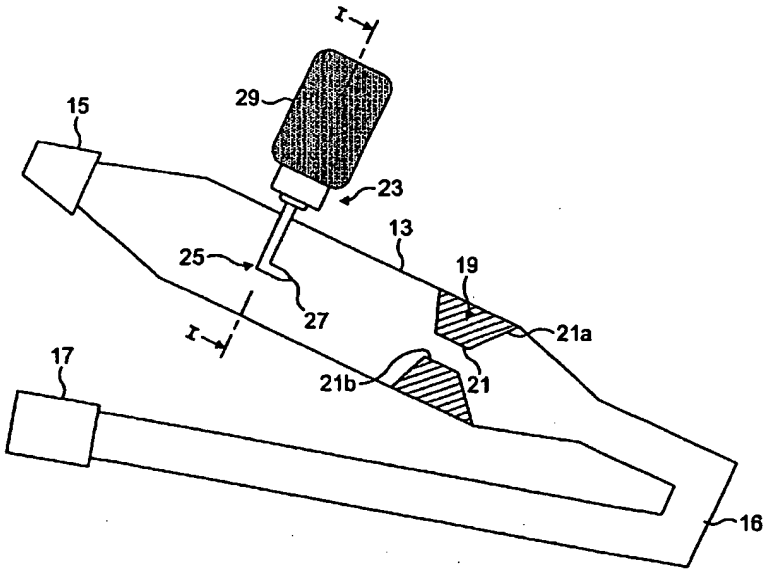

(57) Abstract: A nasal delivery device for delivering substance to a nasal airway of a subject, comprising: a nosepiece (15) for fitting to a nostril of a subject; a chamber (13) fluidly connected to the nosepiece (15) and including a flow regulator (19) for generating a regulated gas stream within the chamber (13) along a flow axis in a flow direction towards the nosepiece (15), wherein the flow regulator (19) is configured to focus and accelerate a gas flow provided thereto and generate a regulated gas stream of increased velocity within the chamber (13) along the flow axis; and a delivery unit (23) comprising a substance supply unit (29) and at least one nozzle (27) fluidly connected to the substance supply unit (29) for delivering at least one aerosol spray into the gas stream.

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NASAL DEVICES

The present invention relates to a nasal delivery device for and a method of delivering substance, in particular one of a liquid, as a suspension or solution, or a powder containing a medicament, especially systemic or topical pharmaceuticals, or a vaccine to the nasal airway of a subject.

Referring to Figure 1, the nasal airway 1 comprises the two nasal cavities 2, 3 separated by the nasal septum 4, which airway 1 includes numerous ostia, such as the paranasal sinus ostia 5 connected to the paranasal sinuses 6 and the tubal ostia 7 connected to the tuba auditiva 8 and the middle ears 9, and olfactory cells, and is lined by the nasal mucosa. The nasal airway 1 can communicate with the nasopharynx, the oral cavity and the lower airway, with the nasal airway 1 being in selective communication with the anterior region of the nasopharynx and the oral cavity by opening and closing of the oropharyngeal velum.

There are many nasal conditions which require treatment. One such condition is nasal inflammation, specifically rhinitis, which can be allergic or non-allergic and is often associated with infection and prevents normal nasal function. By way of example, allergic and non-allergic inflammation of the nasal airway can typically effect between 10 and 20 % of the population, with nasal congestion of the erectile tissues of the nasal concha, lacrimation, secretion of watery mucus, sneezing and itching being the most common symptoms. As will be understood, nasal congestion impedes nasal breathing and promotes oral breathing, leading to snoring and sleep disturbance. Other nasal conditions include nasal polyps which arise from the paranasal sinuses, hypertrophic adenoids, secretory otitis media, sinus disease and reduced olfaction.

In the treatment of certain nasal conditions, the topical administration of medicaments is preferable, particularly where the nasal mucosa is the prime pathological pathway, such as in treating or relieving nasal congestion. Medicaments that are commonly topically delivered include decongestants, anti-histamines, cromoglycates, steroids and antibiotics. At present, among the known anti-inflammatory pharmaceuticals, topical steroids have been shown to have an effect on nasal congestion. Topical decongestants

have also been suggested for use in relieving nasal congestion. The treatment of hypertrophic adenoids and chronic secretory otitis media using topical decongestants, steroids and anti-microbial agents, although somewhat controversial, has also been proposed. Further, the topical administration of pharmaceuticals has been used to treat or at least relieve symptoms of inflammation in the anterior region of the nasopharynx, the paranasal sinuses and the auditory tubes.

Medicaments can also be systemically delivered through the nasal pathway, the nasal pathway offering a good administration route for the systemic delivery of pharmaceuticals, such as hormones, for example, oxytocin and calcitionin, and analgetics, such as anti-migraine compositions, as the high blood flow and large surface area of the nasal mucosa advantageously provides for rapid systemic uptake.

Nasal delivery is also expected to be advantageous for the administration of medicaments requiring a rapid onset of action, for example, analgetics, anti-emetics, insulin, anti-epileptics, sedatives and hypnotica, and also other pharmaceuticals, for example, cardio-vascular drugs. It is envisaged that nasal administration will provide for a fast onset of action, at a rate similar to that of injection and at a rate much faster than that of oral administration. Indeed, for the treatment of many acute conditions, nasal administration is advantageous over oral administration, since gastric stasis can further slow the onset of action following oral administration.

It is also expected that nasal delivery could provide an effective delivery route for the administration of proteins and peptides as produced by modern biotechnological techniques. For such substances, the metabolism in the intestines and the first-pass-effect in the liver represent significant obstacles for reliable and cost-efficient delivery.

Furthermore, it is expected that nasal delivery using the nasal delivery technique of the present invention will prove effective in the treatment of many common neurological diseases, such as Alzheimer's, Parkinson's, psychiatric diseases and intracerebral infections, where not possible using existing techniques. The nasal delivery technique of the present invention allows for delivery to the olfactory region, which region is located in the superior region of the nasal cavities and represents the only region where it is

possible to circumvent the blood-to-brain barrier (BBB) and enable communication with the cerebrospinal fluid (CSF) and the brain.

Also, it is expected that the nasal delivery technique of the present invention will allow for the effective delivery of vaccines.

Aside from the delivery of medicaments and vaccines, the irrigation of the nasal mucosa with liquids, in particular saline solutions, is commonly practised to remove particles and secretions, as well as to improve the mucociliary activity of the nasal mucosa. These solutions can be used in combination with active pharmaceuticals.

For any kind of drug delivery, accurate and reliable dosing is essential, but it is of particular importance in relation to the administration of potent drugs which have a narrow therapeutic window, drugs with potentially serious adverse effects and drugs for the treatment of serious and life-threatening conditions. For some conditions, it is essential to individualize the dosage to the particular situation, for example, in the case of diabetes mellitus. For diabetes, and, indeed, for many other conditions, the dosage of the pharmaceutical is preferably based on actual real-time measurements. Currently, blood samples are most frequently used, but the analysis of molecules in the exhalation breath of subjects has been proposed as an alternative to blood analysis for several conditions. Breath analysis is currently used for the diagnosis of conditions such as helicobacter pylori infections which cause gastric ulcers.

WO-A-00/51672 discloses a delivery device for delivering substance, in particular a medicament, in a bi-directional flow through the nasal cavities, that is, an air flow which passes into one nostril, around the posterior margin of the nasal septum and in the opposite direction out of the other nostril. This bi-directional air flow advantageously acts to stimulate the sensory nerves in the nasal mucosa, thereby conditioning the subject for the delivery and providing a more comfortable delivery situation.

There are many kinds of existing delivery units which are capable of delivering an aerosol spray of substance as required for nasal delivery. Such delivery units include

aerosol canisters as used in pressurized metered dose inhalers (pMDIs) and mechanical delivery pumps, such as liquid spray pumps.

These delivery units are well developed, but, for the purposes of nasal delivery, suffer from the particular disadvantage of the particles of the aerosol spray being projected from the delivery nozzle with a delivery force which is such as not to allow for the aerosol spray to be readily entrained. Indeed, the delivery forces are such that the particles of the aerosol spray would impact, and collect, on any proximate surfaces.

In the field of inhalation technology, spacers have been developed as a means of overcoming this particular problem. Spacers are essentially chambers into which an aerosol spray of substance is delivered and from which the substance is inhaled, typically by a subject inhaling from an outlet port. One such spacer is disclosed in WO-A-92/04065.

It is an aim of the present invention to provide an improved nasal delivery device for and a method of delivering substance to the nasal airway of a subject.

In one aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject, comprising: a nosepiece for fitting to a nostril of a subject; a chamber fluidly connected to the nosepiece and including a flow regulator for generating a regulated gas stream within the chamber along a flow axis in a flow direction towards the nosepiece; and a delivery unit comprising a substance supply unit and a plurality of nozzles fluidly connected to the substance supply unit each for delivering an aerosol spray into the gas stream.

In one embodiment the nozzles of the delivery unit are each configured to deliver an aerosol spray towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

In another embodiment the nozzles of the delivery unit are each configured to deliver an aerosol spray towards the flow axis in a direction substantially orthogonal to the flow direction.

In a further embodiment the nozzles of the delivery unit are each configured to deliver an aerosol spray towards the flow axis in a direction inclined to the flow axis and in the flow direction.

Preferably, the nozzles of the delivery unit are radially disposed about the flow axis.

More preferably, pairs of the nozzles are diametrically opposed.

Preferably, the flow regulator is configured to focus and accelerate a gas flow provided thereto and generate a regulated gas stream of increased velocity within the chamber along the flow axis.

More preferably, the flow regulator comprises a flow passage including a focusing section of decreasing radial dimension in the flow direction, which focusing section acts to focus and accelerate a gas flow supplied thereto.

Yet more preferably, the flow passage includes a delivery section of substantially uniform radial dimension downstream of the focusing section.

Preferably, the delivery device further comprises: a mouthpiece through which the subject in use exhales.

Preferably, the delivery device further comprises: a gas supply channel for supplying a gas flow to the flow regulator.

In one embodiment the mouthpiece is fluidly connected to the gas supply channel, whereby the gas flow is an air flow developed by an exhalation breath of the subject.

In another embodiment the delivery device further comprises: a gas supply unit which is fluidly connected to the gas supply channel for delivering a gas flow through the gas supply channel.

Preferably, the mouthpiece is fluidly connected to the gas supply unit and the gas supply unit is an exhalation breath actuatable unit which is actuated on exhalation by the subject.

In one embodiment the substance supply unit comprises an aerosol canister.

In another embodiment the substance supply unit comprises a delivery pump.

Preferably, the delivery pump comprises a liquid spray pump.

In another aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject, comprising: a nosepiece for fitting to a nostril of a subject; a chamber fluidly connected to the nosepiece and including a flow regulator for generating a regulated gas stream within the chamber along a flow axis in a flow direction towards the nosepiece, wherein the flow regulator is configured to focus and accelerate a gas flow provided thereto and generate a regulated gas stream of increased velocity within the chamber along the flow axis; and a delivery unit comprising a substance supply unit and at least one nozzle fluidly connected to the substance supply unit for delivering at least one aerosol spray into the gas stream.

In one embodiment the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray substantially along the flow axis in a direction opposing the flow direction.

In another embodiment the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

In a further embodiment the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray towards the flow axis in a direction substantially orthogonal to the flow direction.

In a yet further embodiment the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray towards the flow axis in a direction inclined to the flow axis and in the flow direction.

In one embodiment the delivery unit comprises a plurality of nozzles.

Preferably, the nozzles of the delivery unit are radially disposed about the flow axis.

More preferably, pairs of the nozzles are diametrically opposed.

Preferably, the flow regulator comprises a flow passage including a focusing section of decreasing radial dimension in the flow direction, which focusing section acts to focus and accelerate a gas flow supplied thereto.

More preferably, the flow passage includes a delivery section of substantially uniform radial dimension disposed downstream of the focusing section.

Preferably, the delivery device further comprises: a mouthpiece through which the subject in use exhales.

Preferably, the delivery device further comprises: a gas supply channel for supplying a gas flow to the flow regulator.

In one embodiment the mouthpiece is fluidly connected to the gas supply channel, whereby the gas flow is an air flow developed by an exhalation breath of the subject.

In another embodiment the delivery device further comprises: a gas supply unit which is fluidly connected to the gas supply channel for delivering a gas flow through the gas supply channel.

Preferably, the mouthpiece is fluidly connected to the gas supply unit and the gas supply unit is an exhalation breath actuatable unit which is actuated on exhalation by the subject.

In one embodiment the substance supply unit comprises an aerosol canister.

In another embodiment the substance supply unit comprises a delivery pump.

Preferably, the delivery pump comprises a liquid spray pump.

In a further aspect the present invention provides a nasal delivery device for delivering substance to a nasal airway of a subject, comprising: a nosepiece for fitting to a nostril of a subject; a chamber fluidly connected to the nosepiece and including a flow regulator for generating a regulated gas stream in a flow direction within the chamber; and a delivery unit comprising a substance supply unit and at least one nozzle fluidly connected to the substance supply unit for delivering at least one aerosol spray into the gas stream.

In a yet further aspect the present invention provides a method of delivering substance to a nasal airway of a subject, comprising the steps of: fitting a nosepiece to a nostril of a subject; providing a gas flow; generating from the gas flow a regulated gas stream within a chamber along a flow axis in a flow direction towards the nosepiece; and delivering a plurality of aerosol sprays into the gas stream.

In one embodiment the aerosol sprays are delivered towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

In another embodiment the aerosol sprays are delivered towards the flow axis in a direction substantially orthogonal to the flow direction.

In a further embodiment the aerosol sprays are delivered towards the flow axis in a direction inclined to the flow axis and in the flow direction.

In one embodiment the aerosol sprays are delivered radially towards the flow axis.

Preferably, pairs of the aerosol sprays are directed oppositely towards the flow axis.

Preferably, the step of generating a regulated gas stream comprises the step of: focusing and accelerating the gas flow to generate a regulated gas stream of increased velocity within the chamber along the flow axis.

Preferably, the method further comprises the step of: the subject exhaling through a mouthpiece.

In one embodiment the gas flow is an air flow developed by an exhalation breath of the subject.

In another embodiment the gas flow is a gas flow separate to an exhalation breath of the subject.

In one embodiment the aerosol sprays are generated by an aerosol canister.

In another embodiment the aerosol sprays are generated by a spray pump, either as a liquid or powder aerosol spray.

In a still further aspect the present invention provides a method of delivering substance to a nasal airway of a subject, comprising the steps of: fitting a nosepiece to a nostril of a subject; providing a gas flow; focusing and accelerating the gas flow to generate a gas stream of increased velocity within a chamber along a flow axis in a flow direction towards the nosepiece; and delivering at least one aerosol spray into the gas stream.

In one embodiment the at least one aerosol spray is delivered substantially along the flow axis in a direction opposing the flow direction.

In another embodiment the at least one aerosol spray is delivered towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

In a further embodiment the at least one aerosol spray is delivered towards the flow axis in a direction substantially orthogonal to the flow direction.

In a yet further embodiment the at least one aerosol spray is delivered towards the flow axis in a direction inclined to the flow axis and in the flow direction.

In one embodiment the step of delivering at least one aerosol spray into the gas stream comprises the step of: delivering a plurality of aerosol sprays into the gas stream.

Preferably, the aerosol sprays are delivered radially towards the flow axis.

More preferably, pairs of the aerosol sprays are directed oppositely towards the flow axis.

Preferably, the method further comprises the step of: the subject exhaling through a mouthpiece.

In one embodiment the gas flow is an air flow developed by an exhalation breath of the subject.

In another embodiment the gas flow is a gas flow separate to an exhalation breath of the subject.

In one embodiment the at least one aerosol spray is generated by an aerosol canister.

In another embodiment the at least one aerosol spray is generated by a spray pump, either as a liquid or powder aerosol spray.

Preferred embodiments of the present invention will now be described hereinbelow by way of example only with reference to the accompanying drawings, in which:

Figure 1 schematically illustrates the nasal airway of a human subject;

Figure 2(a) schematically illustrates a nasal delivery device in accordance with a first embodiment of the present invention;

Figure 2(b) illustrates a part-sectional view (along section I-I in Figure 2(a)) of the nasal delivery device of Figure 2(a);

Figure 2(c) illustrates the nasal delivery device of Figure 2(a) in the actuated configuration;

Figure 3(a) schematically illustrates a nasal delivery device in accordance with a second embodiment of the present invention;

Figure 3(b) illustrates a part-sectional view (along section II-II in Figure 3(a)) of the nasal delivery device of Figure 3(a);

Figure 3(c) illustrates the nasal delivery device of Figure 3(a) in the actuated configuration;

Figure 4(a) schematically illustrates a nasal delivery device in accordance with a third embodiment of the present invention;

Figure 4(b) illustrates a part-sectional view (along section III-III in Figure 4(a)) of the nasal delivery device of Figure 4(a); and

Figure 4(c) illustrates the nasal delivery device of Figure 4(a) in the actuated configuration.

Figures 2(a) to (c) illustrate a nasal delivery device in accordance with a first embodiment of the present invention.

The delivery device comprises a chamber 13, in this embodiment a tubular member, through which a gas flow, in this embodiment an air flow developed by the exhalation breath of a subject, is delivered, a nosepiece 15 for fitting to a nostril of the subject which is in fluid communication with one, the downstream, end of the chamber 13, a gas supply channel 16, one end of which is in fluid communication with the other, upstream,

end of the chamber 13, and a mouthpiece 17 through which the subject exhales and which is in fluid communication with the other end of the gas supply channel 16.

The chamber 13 includes a flow regulator 19 which is disposed at the other, upstream, end thereof and acts to provide a focused, high-velocity gas stream within the chamber 13 along the longitudinal axis thereof, this being the flow axis of the gas stream. In this embodiment the flow regulator 19 includes a single flow passage 21 which is centered on the longitudinal axis of the chamber 13, and acts to focus and accelerate a gas flow delivered through the gas supply channel 16 and generate a focused, high-velocity gas stream downstream thereof, where the gas stream has a smaller radial dimension than the chamber 13. The flow passage 21 includes a first, focusing section 21a which is of reducing radial dimension in a downstream direction, in this embodiment of frusto-conical section, and acts to focus and accelerate a gas flow delivered through the gas supply channel 16, and a second, delivery section 21b, in this embodiment of cylindrical section, which is disposed downstream of the focusing section 21a and acts to direct the gas stream. In this embodiment the gas stream exiting the flow regulator 19 is substantially turbulent. In another embodiment the flow regulator 19 could be configured to provide a substantially laminar flow, for example, by extending the length of the delivery section 21b of the flow passage 21.

The delivery device further comprises a delivery unit 23 for delivering an aerosol spray of substance into the chamber 13. The delivery unit 23 comprises a nozzle unit 25 which includes a nozzle 27 for delivering an aerosol spray of substance, and a substance supply unit 29 for delivering a metered dose of substance to the nozzle unit 25.

In this embodiment the nozzle 27 of the nozzle unit 25 faces in a direction upstream of the nosepiece 15, that is, in a direction opposing the gas flow through the chamber 13, and is disposed so as to be co-axial with the flow axis, that is, the longitudinal axis of the flow passage 21 of the flow regulator 19, whereby an aerosol spray, when delivered from the nozzle 27, is acted upon by the high-velocity gas stream exiting the flow regulator 19 such as to rapidly decelerate the particles of the aerosol spray, which particles, once decelerated, are then entrained by the gas flow through the chamber 13.

In other embodiments the nozzle 27 of the nozzle unit 25 could face in other directions, typically orthogonally to the flow axis or in the direction of the nosepiece 15.

In this embodiment the substance supply unit 29 is an aerosol canister for delivering a metered volume of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing a medicament, either as a suspension or solution.

The substance supply unit 29 is primeable, in this embodiment by loading a biasing element, and includes a release mechanism, which, when triggered, releases the biasing element and actuates the substance supply unit 29 to deliver a metered dose of substance.

In an alternative embodiment the substance supply unit 29 could comprise a mechanical delivery pump, in particular a liquid delivery pump or a powder delivery pump, which delivers metered doses of substance on actuation thereof.

Operation of the delivery device will now be described hereinbelow.

Firstly, the nosepiece 15 is fitted to a nostril of a subject and the mouthpiece 17 is gripped in the lips of the subject.

The subject then begins to exhale through the mouthpiece 17, which exhalation acts to close the oropharyngeal velum of the subject and deliver a gas flow through the gas supply channel 16, the chamber 13 and the nasal airway 1 of the subject, which gas flow is focused and accelerated by the flow regulator 19 at the upstream end of the chamber 13 to provide a focussed, high-velocity gas stream.

The subject then actuates the substance supply unit 29 to deliver a metered dose of substance through the nozzle 27 of the nozzle unit 25, which nozzle 27 generates an aerosol spray in a direction opposing the direction of the high-velocity gas stream from the flow regulator 19. The aerosol spray, when delivered from the nozzle 27, is acted upon by the high-velocity gas stream exiting the flow regulator 19 such as to rapidly

decelerate the particles of the aerosol spray, which particles, once decelerated, are then entrained by the gas flow through the chamber 13.

In this way, the particles of the generated aerosol as delivered to the nasal airway 1 have the same velocity as the entraining gas flow, and thus deposition on unwanted surfaces, which would result where the particles are delivered directly to the nosepiece 15, is avoided.

Figures 3(a) to (c) illustrate a nasal delivery device in accordance with a second embodiment of the present invention.

The delivery device of this embodiment is very similar to the delivery device of the above-described first embodiment, and thus, in order to avoid unnecessary duplication of description, only the differences will be described in detail, with like reference signs designating like parts

The delivery device of this embodiment differs from that of the above-described first embodiment in further comprising an exhalation breath actuatable gas supply unit 31 for delivering a gas flow through the gas supply channel 16 to the chamber 13 in response to exhalation by a subject, and in that the mouthpiece 17 is in fluid communication with the gas supply unit 31 and not the chamber 13, whereby a gas flow is delivered to the chamber 13, and hence the nasal airway 1, by the gas supply unit 31 in response to exhalation through the mouthpiece 17.

Operation of the delivery device is the same as for the above-described first embodiment, with a gas flow being delivered to the chamber 13, and hence the nasal airway 1, by the gas supply unit 31 in response to exhalation through the mouthpiece 17, with the gas flow being delivered to the chamber 13 as a high-velocity gas stream.

Figures 4(a) to (c) illustrate a nasal delivery device in accordance with a third embodiment of the present invention.

The delivery device comprises a chamber 43, in this embodiment a tubular member, through which a gas flow, in this embodiment an air flow developed by the exhalation breath of a subject, is delivered, a nosepiece 45 for fitting to a nostril of the subject which is in fluid communication with one, the downstream, end of the chamber 43, a gas supply channel 46, one end of which is in fluid communication with the other, upstream, end of the chamber 43, and a mouthpiece 47 through which the subject exhales and which is in fluid communication with the other end of the gas supply channel 46.

The chamber 43 includes a flow regulator 49 which is disposed at the other, upstream, end thereof and acts to provide a focused, high-velocity gas stream within the chamber 43 along the longitudinal axis thereof, this being the flow axis of the gas stream. In this embodiment the flow regulator 49 includes a single flow passage 51 which is centered on the longitudinal axis of the chamber 43, and acts to focus and accelerate a gas flow delivered through the gas supply channel 46 and generate a focused, high-velocity gas stream downstream thereof, where the gas stream has a smaller radial dimension than the chamber 13. The flow passage 51 includes a first, focusing section 51a which is of reducing radial dimension in a downstream direction, in this embodiment of frusto-concave section, and acts to focus and accelerate a gas flow delivered through the gas supply channel 46, and a second, delivery section 51b, in this embodiment of cylindrical section, which is disposed downstream of the focusing section 51a and acts to direct the gas stream. In this embodiment the gas stream exiting the flow regulator 49 is substantially turbulent. In another embodiment the flow regulator 49 could be configured to provide a substantially laminar flow, for example, by extending the length of the delivery section 51b of the flow passage 51.

The delivery device further comprises a delivery unit 53 for delivering aerosol sprays of substance into the chamber 43. The delivery unit 53 comprises a nozzle unit 55 which includes a plurality of nozzles 57, in this embodiment four nozzles 57 disposed about the periphery of the chamber 43, for delivering aerosol sprays of substance, and a substance supply unit 59 for delivering a metered dose of substance to the nozzle unit 55.

In this embodiment the nozzles 57 of the nozzle unit 55 are equi-angularly spaced, that is, at 90 degree intervals, and face inwardly in a direction substantially orthogonal to the

flow direction of the gas stream, whereby aerosol sprays, when delivered from the nozzles 57, are acted upon by the high-velocity gas stream exiting the flow regulator 49 such as to be deflected in the flow direction of the gas flow through the chamber 43. In deflecting the particles of the aerosol spray, the particles are rapidly decelerated and entrained by the gas flow through the chamber 43. Also, where pairs of the nozzles 57 of the nozzle unit 55 are diametrically opposed, the aerosol sprays delivered by those nozzles 57 impinge on one another and cause deceleration of the particles of the aerosol sprays. In other embodiments the nozzles 57 of the nozzle unit 55 could be inclined relative to the flow axis of the gas stream such as to be directed in an upstream or downstream direction.

In this embodiment the substance supply unit 59 is an aerosol canister for delivering a metered volume of a propellant, preferably a hydrofluoroalkane (HFA) propellant or the like, containing a medicament, either as a suspension or solution.

The substance supply unit 59 is primeable, in this embodiment by loading a biasing element, and includes a release mechanism, which, when triggered, releases the biasing element and actuates the substance supply unit 59 to deliver a metered dose of substance.

In an alternative embodiment the substance supply unit 59 could comprise a mechanical delivery pump, in particular a liquid delivery pump or a powder delivery pump, which delivers metered doses of substance on actuation thereof.

Operation of the delivery device will now be described hereinbelow.

Firstly, the nosepiece 45 is fitted to a nostril of a subject and the mouthpiece 47 is gripped in the lips of the subject.

The subject then begins to exhale through the mouthpiece 47, which exhalation acts to close the oropharyngeal velum of the subject and deliver a gas flow through the gas supply channel 46, the chamber 43 and the nasal airway 1 of the subject, which gas flow

is focused and accelerated by the flow regulator 49 at the upstream end of the chamber 43 to provide a focussed, high-velocity gas stream.

The subject then actuates the substance supply unit 59 to deliver a metered dose of substance through the nozzles 57 of the nozzle unit 55, which nozzles 57 generate aerosol sprays in a direction substantially orthogonal to the high-velocity gas stream developed in the chamber 43 by the flow regulator 49. The aerosol sprays, when delivered from the nozzles 57, are acted upon by the high-velocity gas stream developed by the flow regulator 49 such as to be deflected in the flow direction through the chamber 43. The deflected particles of the aerosol sprays are rapidly decelerated and entrained by the gas flow through the chamber 43.

In this way, the particles of the generated aerosol as delivered to the nasal airway 1 have the same velocity as the entraining gas flow, and thus deposition on unwanted surfaces, which would result where the particles are delivered directly to the nosepiece 45, is avoided.

Finally, it will be understood that the present invention has been described in its preferred embodiments and can be modified in many different ways without departing from the scope of the invention as defined by the appended claims.

For example, the nasal delivery device of the above-described third embodiment could be modified in the manner of the above-described second embodiment, that is, to include an exhalation breath actuatable gas supply unit 31 for delivering a gas flow through the chamber 43 which is separate to the exhalation breath of a subject.

CLAIMS

1. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:

a nosepiece for fitting to a nostril of a subject;

a chamber fluidly connected to the nosepiece and including a flow regulator for generating a regulated gas stream within the chamber along a flow axis in a flow direction towards the nosepiece; and

a delivery unit comprising a substance supply unit and a plurality of nozzles fluidly connected to the substance supply unit each for delivering an aerosol spray into the gas stream.

2. The delivery device of claim 1, wherein the nozzles of the delivery unit are each configured to deliver an aerosol spray towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

3. The delivery device of claim 1, wherein the nozzles of the delivery unit are each configured to deliver an aerosol spray towards the flow axis in a direction substantially orthogonal to the flow direction.

4. The delivery device of claim 1, wherein the nozzles of the delivery unit are each configured to deliver an aerosol spray towards the flow axis in a direction inclined to the flow axis and in the flow direction.

5. The delivery device of any of claims 1 to 4, wherein the nozzles of the delivery unit are radially disposed about the flow axis.

6. The delivery device of claim 5, wherein pairs of the nozzles are diametrically opposed.

7. The delivery device of any of claims 1 to 6, wherein the flow regulator is configured to focus and accelerate a gas flow provided thereto and generate a

regulated gas stream of increased velocity within the chamber along the flow axis.

8. The delivery device of claim 7, wherein the flow regulator comprises a flow passage including a focusing section of decreasing radial dimension in the flow direction, which focusing section acts to focus and accelerate a gas flow supplied thereto.

9. The delivery device of claim 8, wherein the flow passage includes a delivery section of substantially uniform radial dimension downstream of the focusing section.

10. The delivery device of any of claims 1 to 9, further comprising:
a mouthpiece through which the subject in use exhales.

11. The delivery device of any of claims 1 to 10, further comprising:
a gas supply channel for supplying a gas flow to the flow regulator.

12. The delivery device of claim 11 when appendant upon claim 10, wherein the mouthpiece is fluidly connected to the gas supply channel, whereby the gas flow is an air flow developed by an exhalation breath of the subject.

13. The delivery device of claim 11, further comprising:
a gas supply unit which is fluidly connected to the gas supply channel for delivering a gas flow through the gas supply channel.

14. The delivery device of claim 13 when appendant upon claim 10, wherein the mouthpiece is fluidly connected to the gas supply unit and the gas supply unit is an exhalation breath actuatable unit which is actuated on exhalation by the subject.

15. The delivery device of any of claims 1 to 14, wherein the substance supply unit comprises an aerosol canister.

16. The delivery device of any of claims 1 to 14, wherein the substance supply unit comprises a delivery pump.

17. The delivery device of claim 16, wherein the delivery pump comprises a liquid spray pump.

18. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:

a nosepiece for fitting to a nostril of a subject;

a chamber fluidly connected to the nosepiece and including a flow regulator for generating a regulated gas stream within the chamber along a flow axis in a flow direction towards the nosepiece, wherein the flow regulator is configured to focus and accelerate a gas flow provided thereto and generate a regulated gas stream of increased velocity within the chamber along the flow axis; and

a delivery unit comprising a substance supply unit and at least one nozzle fluidly connected to the substance supply unit for delivering at least one aerosol spray into the gas stream.

19. The delivery device of claim 18, wherein the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray substantially along the flow axis in a direction opposing the flow direction.

20. The delivery device of claim 18, wherein the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

21. The delivery device of claim 18, wherein the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray towards the flow axis in a direction substantially orthogonal to the flow direction.

22. The delivery device of claim 18, wherein the at least one nozzle of the delivery unit is configured to deliver at least one aerosol spray towards the flow axis in a direction inclined to the flow axis and in the flow direction.

23. The delivery device of any of claims 18 to 22, wherein the delivery unit comprises a plurality of nozzles.

24. The delivery device of claim 23, wherein the nozzles of the delivery unit are radially disposed about the flow axis.

25. The delivery device of claim 24, wherein pairs of the nozzles are diametrically opposed.

26. The delivery device of any of claims 18 to 25, wherein the flow regulator comprises a flow passage including a focusing section of decreasing radial dimension in the flow direction, which focusing section acts to focus and accelerate a gas flow supplied thereto.

27. The delivery device of claim 26, wherein the flow passage includes a delivery section of substantially uniform radial dimension downstream of the focusing section.

28. The delivery device of any of claims 18 to 27, further comprising:
a mouthpiece through which the subject in use exhales.

29. The delivery device of any of claims 18 to 28, further comprising:
a gas supply channel for supplying a gas flow to the flow regulator.

30. The delivery device of claim 29 when appendant upon claim 28, wherein the mouthpiece is fluidly connected to the gas supply channel, whereby the gas flow is an air flow developed by an exhalation breath of the subject.

31. The delivery device of claim 29, further comprising:

a gas supply unit which is fluidly connected to the gas supply channel for delivering a gas flow through the gas supply channel.

32. The delivery device of claim 31 when appendant upon claim 28, wherein the mouthpiece is fluidly connected to the gas supply unit, and the gas supply unit is an exhalation breath actuatable unit which is actuated on exhalation by the subject.

33. The delivery device of any of claims 18 to 32, wherein the substance supply unit comprises an aerosol canister.

34. The delivery device of any of claims 18 to 32, wherein the substance supply unit comprises a delivery pump.

35. The delivery device of claim 34, wherein the delivery pump comprises a liquid spray pump.

36. A nasal delivery device for delivering substance to a nasal airway of a subject, comprising:
a nosepiece for fitting to a nostril of a subject;
a chamber fluidly connected to the nosepiece and including a flow regulator for generating a regulated gas stream in a flow direction within the chamber; and
a delivery unit comprising a substance supply unit and at least one nozzle fluidly connected to the substance supply unit for delivering at least one aerosol spray into the gas stream.

37. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
fitting a nosepiece to a nostril of a subject;
providing a gas flow;
generating from the gas flow a regulated gas stream within a chamber along a flow axis in a flow direction towards the nosepiece; and
delivering a plurality of aerosol sprays into the gas stream.

38. The method of claim 37, wherein the aerosol sprays are delivered towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

39. The method of claim 37, wherein the aerosol sprays are delivered towards the flow axis in a direction substantially orthogonal to the flow direction.

40. The method of claim 37, wherein the aerosol sprays are delivered towards the flow axis in a direction inclined to the flow axis and in the flow direction.

41. The method of any of claims 37 to 40, wherein the aerosol sprays are delivered radially towards the flow axis.

42. The method of claim 41, wherein pairs of the aerosol sprays are directed oppositely towards the flow axis.

43. The method of any of claims 37 to 42, wherein the step of generating a regulated gas stream comprises the step of:
focusing and accelerating the gas flow to generate a regulated gas stream of increased velocity within the chamber along the flow axis.

44. The method of any of claims 37 to 43, further comprising the step of:
the subject exhaling through a mouthpiece.

45. The method of claim 44, wherein the gas flow is an air flow developed by an exhalation breath of the subject.

46. The method of any of claims 37 to 44, wherein the gas flow is a gas flow separate to an exhalation breath of the subject.

47. The method of any of claims 37 to 46, wherein the aerosol sprays are generated by an aerosol canister.

48. The method of any of claims 37 to 46, wherein the aerosol sprays are generated by a spray pump.

49. A method of delivering substance to a nasal airway of a subject, comprising the steps of:
fitting a nosepiece to a nostril of a subject;
providing a gas flow;
focusing and accelerating the gas flow to generate a gas stream of increased velocity within a chamber along a flow axis in a flow direction towards the nosepiece; and
delivering at least one aerosol spray into the gas stream.

50. The method of claim 49, wherein the at least one aerosol spray is delivered substantially along the flow axis in a direction opposing the flow direction.

51. The method of claim 49, wherein the at least one aerosol spray is delivered towards the flow axis in a direction inclined to the flow axis and opposing the flow direction.

52. The method of claim 49, wherein the at least one aerosol spray is delivered towards the flow axis in a direction substantially orthogonal to the flow direction.

53. The method of claim 49, wherein the at least one aerosol spray is delivered towards the flow axis in a direction inclined to the flow axis and in the flow direction.

54. The method of any of claims 49 to 53, wherein the step of delivering at least one aerosol spray into the gas stream comprises the step of:
delivering a plurality of aerosol sprays into the gas stream.

55. The method of claim 54, wherein the aerosol sprays are delivered radially towards the flow axis.

56. The method of claim 55, wherein pairs of the aerosol sprays are directed oppositely towards the flow axis.

57. The method of any of claims 49 to 56, further comprising the step of:
the subject exhaling through a mouthpiece.

58. The method of claim 57, wherein the gas flow is an air flow developed by an exhalation breath of the subject.

59. The method of any of claims 49 to 57, wherein the gas flow is a gas flow separate to an exhalation breath of the subject.

60. The method of any of claims 49 to 59, wherein the at least one aerosol spray is generated by an aerosol canister.

61. The method of any of claims 49 to 59, wherein the at least one aerosol spray is generated by a spray pump.

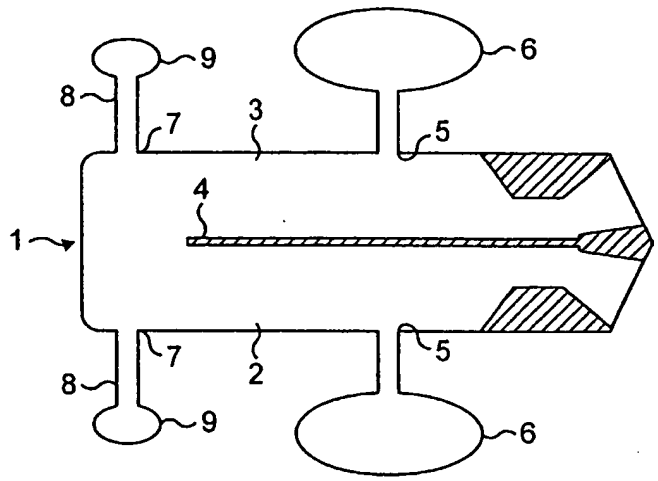

FIG. 1

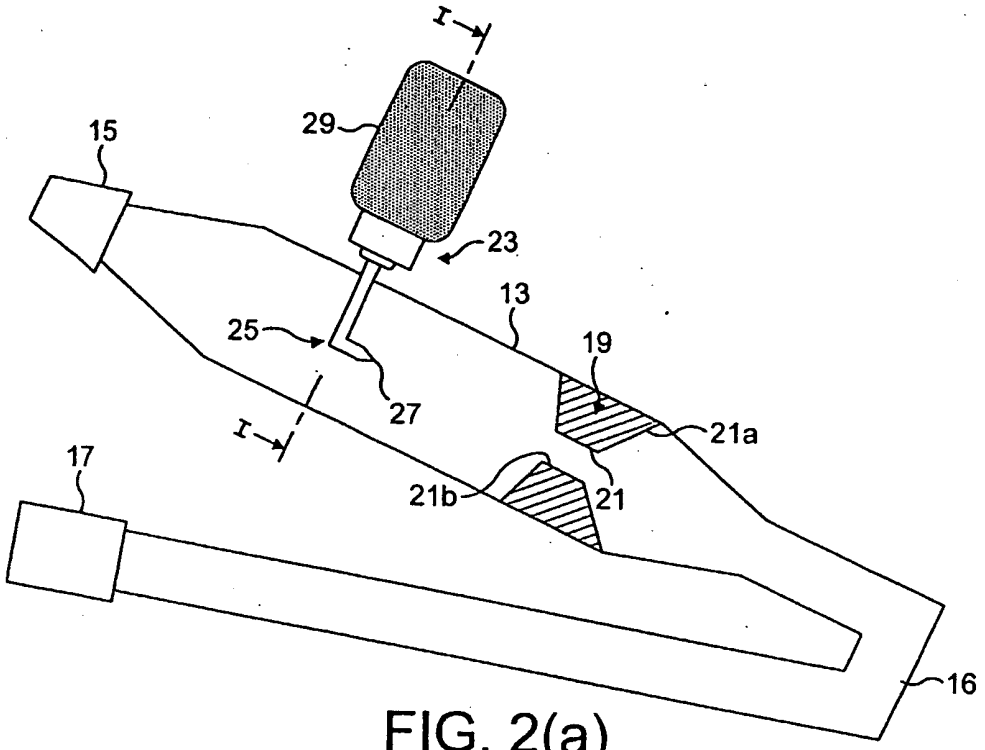

FIG. 2(a)

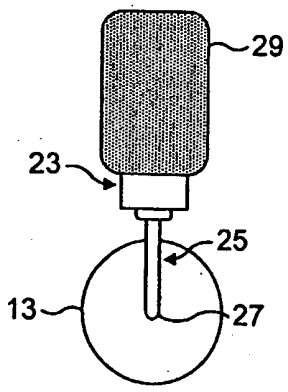

FIG. 2(b)

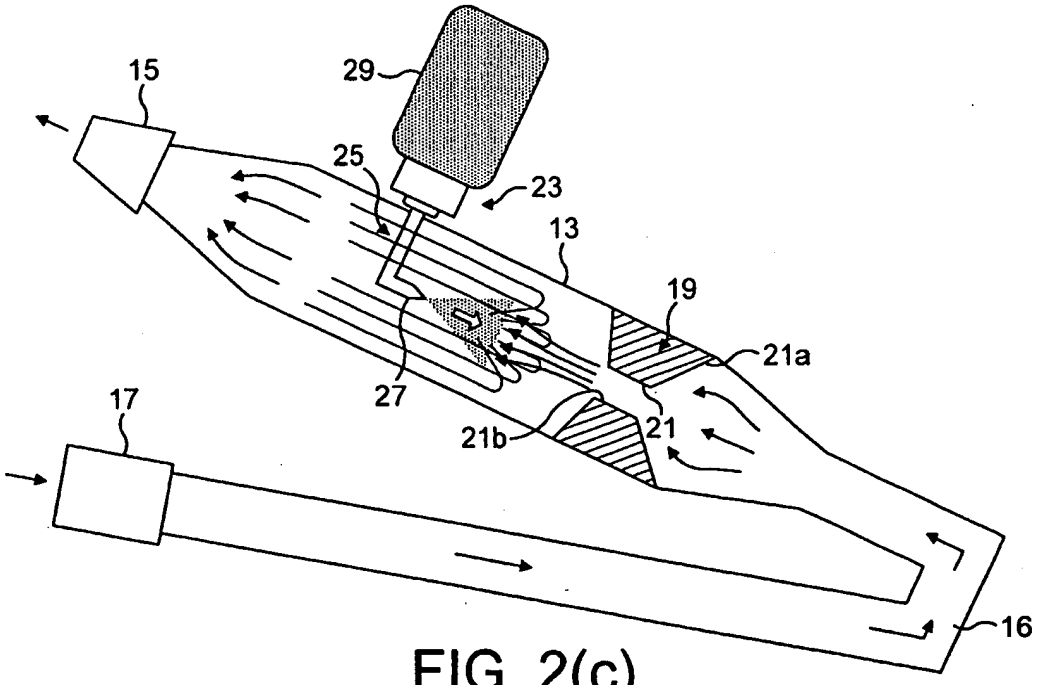

FIG. 2(c)

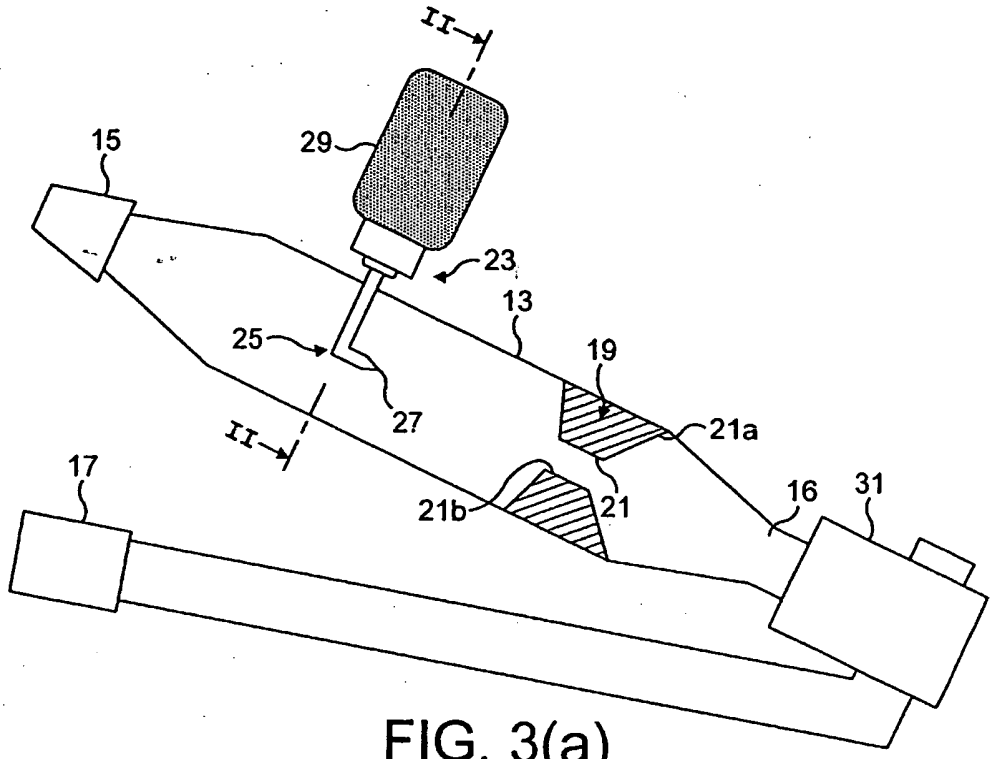

FIG. 3(a)

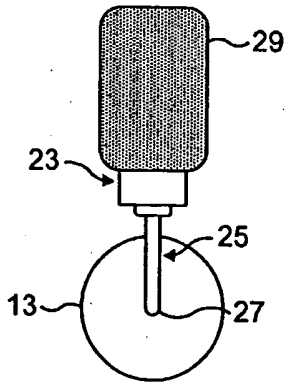

FIG. 3(b)

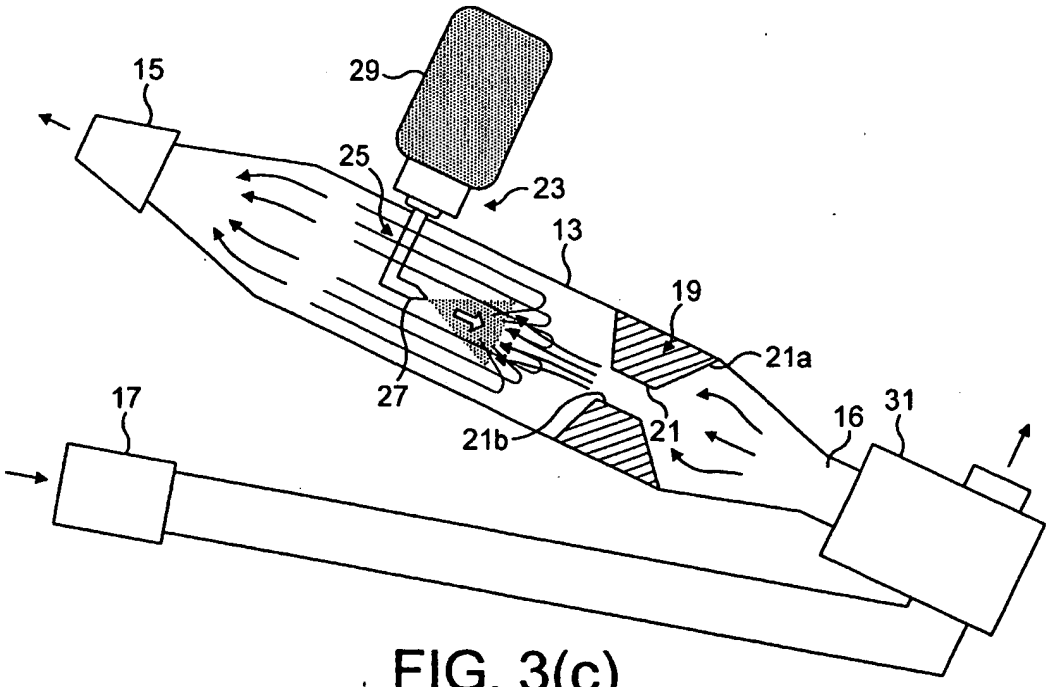

FIG. 3(c)

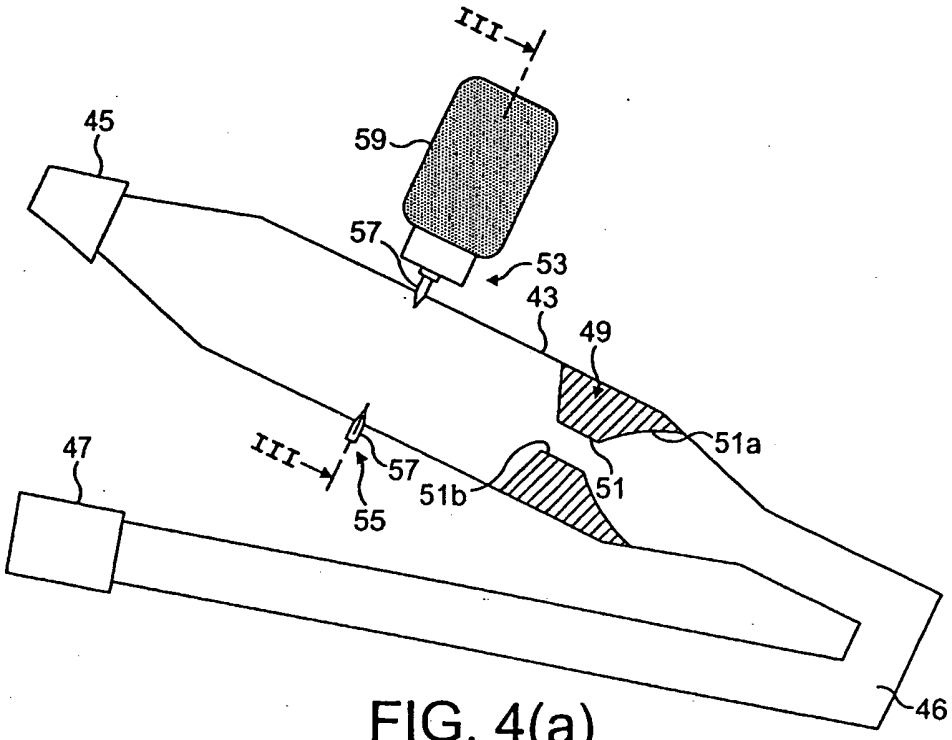
III
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FIG. 4(a)

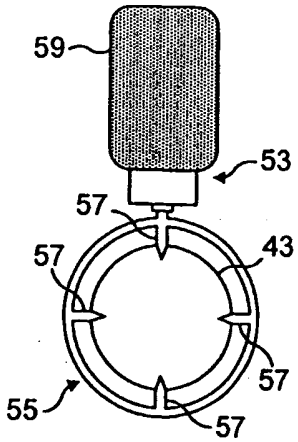
59
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FIG. 4(b)

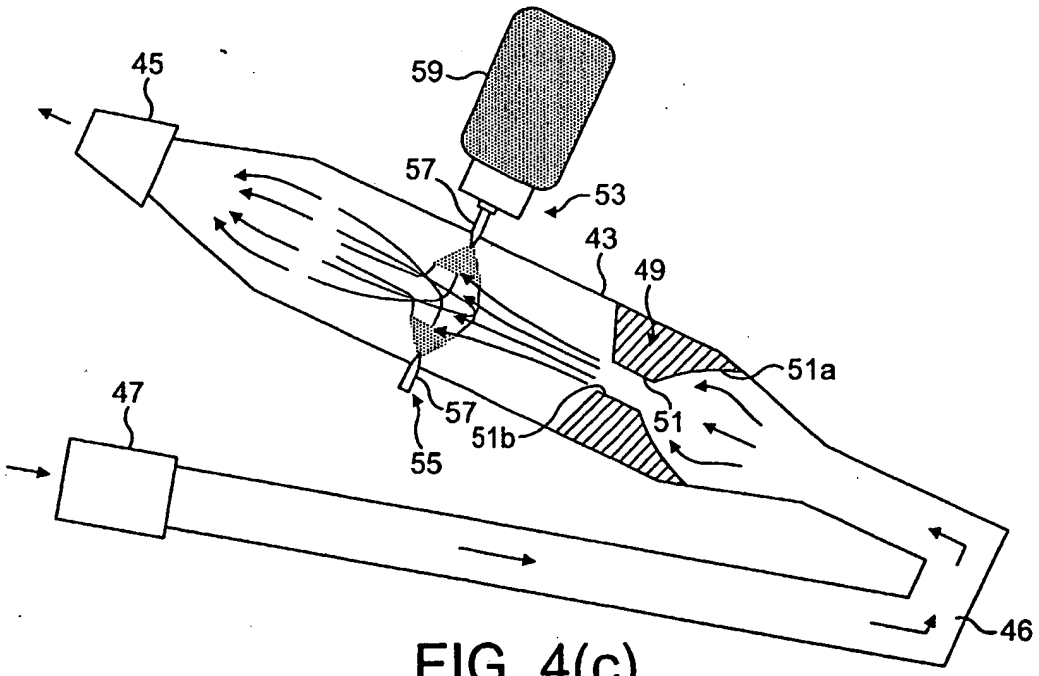

FIG. 4(c)

INTERNATIONAL SEARCH REPORT

In nal Application No
PCT/IB 03/01785

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M16/06 A61M15/00 A61M15/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO 00 51672 A (DJUPESLAND PER GISLE) 8 September 2000 (2000-09-08) cited in the application page 28, line 24 -page 31, line 7; figure 9	36 1-15,18, 21-33
Y	CA 2 207 219 A (MANKOWSKI LESZEK MARION) 19 December 1998 (1998-12-19) page 1, last paragraph -page 3, paragraph 6; figures 1-17	1,2,4, 7-15,18, 22,23, 26-33
Y	US 5 007 419 A (WEINSTEIN ALLAN ET AL) 16 April 1991 (1991-04-16) column 3, line 3 -column 4, line 23; figures 1-3	3,5,6, 21,23-25

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 September 2003	10/09/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Zeinstra, H

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

In nal Application No
PCT/IB 03/01785

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 2 470 297 A (FIELDS MACK R) 17 May 1949 (1949-05-17) column 2, line 47 -column 3, line 50; figures 1-6	1
A	WO 92 04065 A (WALSTROM DENNIS R ;MASLONKA STEVEN R (US); SCOLES WADE J (US)) 19 March 1992 (1992-03-19) cited in the application page 8, last paragraph page 11, last paragraph -page 14, paragraph 1; figures 2-5	19,20
A	US 6 302 101 B1 (PY DANIEL) 16 October 2001 (2001-10-16) column 6, line 35 - line 41; figures 15-17	16,17, 34,35

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-17

   Device with a plurality of nozzles

2. Claims: 18-36

   Device with a flow regulator

INTERNATIONAL SEARCH REPORT

ıational application No.
PCT/IB 03/01785

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 37-61
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Ir bnal Application No
PCT/IB 03/01785

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